New Drugs in 2013

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KEYWORDS

• Drugs • Food and Drug Administration • 2013 • Oncology • Hepatitis • Diabetes • Pulmonary hypertension

KEY POINTS

- Twenty-seven new drugs were approved by the Food and Drug Administration in 2013 with one-third being the first drugs in their class and the majority targeting cancer.
- Canagliflozin represents a new class of medication for diabetes, which may be a useful primary medication.
- There are many new hepatitis C drugs being released in the near future with high likelihood of achieving sustained virologic response.
- Macitentan and riociguat may be new medications that affect mortality in pulmonary hypertension.

INTRODUCTION

In 2013, 27 new drugs (25 small molecules, 2 biologics) were approved by the US Food and Drug Administration (FDA), many with novel mechanisms for the treatment of medical problems often encountered in hospital medicine. Although many of the drugs approved are not routinely prescribed by hospitalists, many hospitalists take care of patients receiving them. Of the drugs approved, 30% were for treatment of oncologic diagnoses and approximately one-third were orphan drugs, the first in their class.[1] Six drugs were chosen to highlight some of the more interesting medications to be released that may soon become familiar to the current hospitalist. They include drugs for metabolic diseases (canagliflozin for diabetes), infectious disease (sofosbuvir for hepatitis C), oncologic diagnoses (ibrutinib for chronic lymphocytic leukemia [CLL]), vascular disease (macitentan and riociguat for pulmonary hypertension), and neurologic disease (dimethyl fumarate for multiple sclerosis).

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CANAGLIFLOZIN

Background

An estimated 25 million adults in the United States have diabetes mellitus. There are many oral drugs on the market designed to achieve glycemic control in patients, with diverse mechanisms of action for achieving this goal. Many of the available options have risks of hypoglycemia, and decrease hemoglobin A_{1c} (HbA_{1c}) levels by only small amounts. Canaglifozin (Invokana) is a sodium-glucose cotransporter 2 (SGLT2) inhibitor, which works by blocking reabsorption of glucose filtered in the kidney, leading to glucosuria. Its mechanism is novel, in that it does not target insulin resistance or secretion, in turn lessening the risk of hypoglycemia and improving the fasting and postprandial glucose level. There are also reports that SGLT2 inhibitors may have the added effect of decreasing blood pressure and potentially promoting weight loss. There are many SGLT2 inhibitors in development for type 2 diabetes, designed to achieve glycemic control and decrease HbA_{1c} levels. Canagliflozin, along with the recently approved dapagliflozin, are the only SGLT2 inhibitors approved by the FDA.

Results from Relevant Studies

All studies looking into canagliflozin have evaluated its use in type 2 diabetes. A recent randomized, double-blind, placebo-controlled study[2] compared 100 mg, 300 mg, or placebo, with a primary end point of change in HbA_{1c} levels. At 26 weeks, HbA_{1c} levels were significantly reduced from baseline in the canaglifozin arms (−0.91% in 100-mg dosing and −1.16% at 300-mg dosing). In addition, both doses significantly decreased fasting plasma glucose and 2-hour postprandial glucose level, body weight, and systolic blood pressure. Both doses were also associated with increased rate of urinary tract infections and genital mycotic infections. Another study adding canagliflozin to insulin therapy[3] showed low rates of hypoglycemia and enhanced decrease of HbA_{1c} levels, although this needs to be further investigated in larger studies.

Commentary

Canagliflozin represents a potentially useful new therapy in those with mild and moderate type 2 diabetes. The optimal dosing has not yet been determined, and it is also not yet known whether monotherapy with this drug or with other drugs, including insulin, is most beneficial. It is currently approved by the FDA at doses of 100 mg and 300 mg, similar to the studies discussed earlier. Given the action on the kidney, its use in those with concurrent renal failure has not yet been fully outlined. Furthermore, whether SGLT2 inhibitors are of use in those with type 1 diabetes has not yet been elucidated.[4] More studies are needed to further outline these issues, but SGLT2 inhibitors seem to add a new option, with the potential to alter the natural course of insulin resistance in diabetes.

SOFOSBUVIR

Background

Hepatitis C afflicts 150 million people worldwide, including 3.2 million individuals in the United States. The novel drug, sofosbuvir (Sovaldi), an RNA polymerase inhibitor, is the first of many drugs in the pipeline that offer a potential interferon-free, all-oral treatment regimen for the treatment of hepatitis C. The usual use of interferon and ribavirin for the treatment of hepatitis C offers not only long treatment courses with variable effectiveness but significant side effects, which prohibit some patients from undergoing therapy at all. For those who do undertake the therapy, completing treatment